DOI: 10.1002/adsc.200900013

Stereoselectivity in the Rhodium-Catalysed Reductions of Non-Conjugated Dienes

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Received: January 10, 2009; Published online: April 16, 2009

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.200900013.

Abstract: The stereochemical course of rhodium-catalysed addition of hydrogen and catecholborane to bicyclo[2.2.1]heptadiene, and of hydrogen to a range of cyclic dienes has been analysed. For hydroboration, the overall catalytic reaction possesses *exo*-selectivity, but the initial step is *endo*-selective. For hydrogenation (deuteration), the first step may occur with either *exo*- or *endo*- selectivity, depending on the structure of the diene. This enables a distinction to be made between pathways involving prior dissociation of the diene, and direct addition to the complexed diene without full dissociation. The relative ease of hydrogenation of the first and second double bonds varies markedly with reactant structure, and also depends on the choice of catalyst ligands. For dicyclopentadiene, hydrogenation of the cyclopentene double bond is accompanied by rapid alkene isomerisation, as revealed by deuterium addition. The asymmetric hydrogenation of acyclic skipped *meso*-dienes is reported, demonstrating control of relative rates of the two sequential steps, with *ee*s of up to 53% after the first reduction.

Keywords: dienes; hydroboration; hydrogenation; rhodium; stereoselectivity

Introduction

Depending on the structure of the reactant, product and catalyst, hydrogenation and other catalysed reactions of an alkene may exhibit diastereo-, regio- or enantioselectivity. For a dialkene, the chemoselectivity of the first step requires additional consideration. In many cases, the desired selectivity is obtained by involvement of a neighbouring directing group that engages the metal in chelate binding.[1] In the present context, our interest lay in the hydrogenation of non-conjugated dienes, where there is the potential to employ one double bond as directing group, exerting stereochemical control of reagent addition to the other. This paper presents exploratory work in cyclic systems, examining the course of addition as a function of diene structure. A preliminary investigation into the asymmetric hydrogenation of acyclic *meso*-alkenes is reported.

Metal-catalysed additions to both bicyclo-[2.2.1]heptadiene **1** and the related monoene **2** have been studied with a range of reagents. Norbornadiene (NBD) can exhibit varied behaviour, whereas reagents invariably add from the *exo*-direction to norbornene (NBE).[2] The first case to be studied was the Rh complex-catalysed hydroformylation of NBE, where *exo*-selectivity prevailed.[3] This was endorsed and extended to Pt complex-catalysed hydroformylation, and NBD was also shown to hydroformylate predominantly but not exclusively at the *exo*-face. It was also demonstrated that *cis*-addition of D_2/CO to NBE occurred.[4] An efficient *exo*-specific Rh-catalysed asymmetric hydroformylation of NBE has been demonstrated.[5] These results contrast with chelation-promoted Rh complex-catalysed hydroacylation of alkenes with salicylaldehyde. *endo*-Hydroacylation of NBD occurs, whereas *exo*-addition occurs to NBE, both with high selectivity.[6] In an extensive search for an enantioselective variant, Bolm and co-workers found wide variability in the stereochemical course of the hydroacylation of NBD, with Rh phosphoramidite complexes *endo*-selective but diphosphine complexes giving both *exo*- and *endo*-diastereoisomers. Related reactions with NBE were *exo*-selective.[7] Hydroamidation,[8] catalytic or stoichiometric hydroboration,[9] asymmetric hydrosilylation,[10] hydroamination with iridium or rhodium,[11] gold,[12] or platinum complexes,[13] C–H addition of terminal alkynes,[14] and

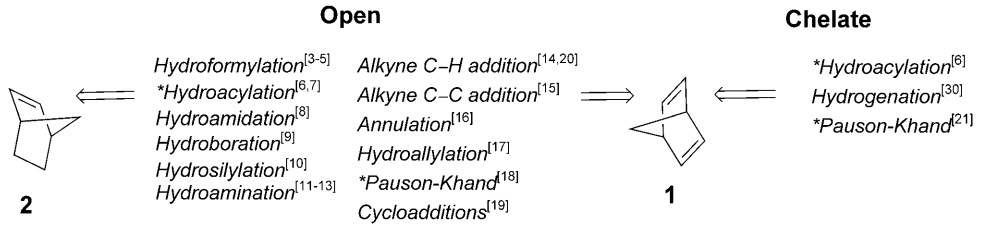


Figure 1. Stereochemical course of catalytic addition reactions to norbornadiene **1** and norbornene **2**.

catalysed alkyne cycloaddition,[15] and catalytic annulation,[16] of NBE are all *exo*-selective. Several of these reactions give *exo*-specific addition with norbornadiene as well.[10,11,16] The main product reported during Rh complex-catalysed asymmetric hydroboration/oxidation of NBD is the *exo-exo*-2,6-diol. *exo*-Addition to norbornadiene occurs in hydroallylation with allyl formate,[17] some Pauson–Khand reactions,[18] Ru-catalysed cycloadditions,[19] and terminal alkyne additions.[20] Aside from the hydroacylations and hydrogenation described above, only the Pauson–Khand reaction with enynes is *endo*-selective.[21] Hence all catalysed additions to norbornene are *exo*-selective, and a clear majority of additions to norbornadiene are likewise. These results are summarised in Figure 1.

The general consistency of results obtained with NBE **2** is in accord with the preferred *exo*-complexation of the alkene that is observed in structurally characterised complexes.[22] These include at least one example for which the bridging methylene group provides an agostic C–H interaction with the metal centre,[23] and one with an agostic Pt–H–C1 arrangement.[24] The variable behaviour of NDB **1** is more intriguing. Preferred bidentate *endo*-coordination of NBD in transition metal complexes is well established, and exemplified in the common precatalysts for rhodium asymmetric hydrogenation. In rarer examples where NBD is singly η^2-coordinated to Ag, Cu or Mn, bonding invariably occurs to the *exo*-face.[25] This implies that the stereochemical course of addition to NBD reveals whether one or both double bonds are coordinated during the transfer process.

Results and Discussion

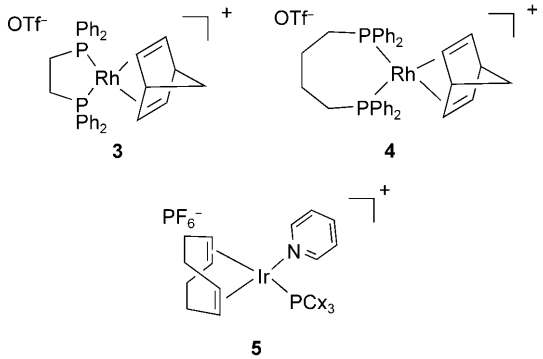
In the following sections a comparison of the addition of hydrogen and secondary boron hydrides to norbornadiene **1** is discussed first, followed by a survey of the course of hydrogenation of non-conjugated cyclic dienes. The final section concerns the asymmetric hydrogenation of an acyclic skipped diene.

Hydrogenation *versus* Hydroboration of Bicyclo[2.2.1]heptadienes

Hydrogenation of NBD

Norbornadiene **1** (NBD) and cycloocta-1,5-diene (COD) feature almost equally as stabilising ligands in precatalysts for rhodium asymmetric hydrogenations. For this reason considerable attention has been given to the reaction step that liberates the active catalyst, normally a diphosphine-rhodium solvate.[26] Since the reduction of norbornadiene is normally much the faster of the two, claims and counterclaims have been made about their relative efficiency as precursor ligands in hydrogenation. On a laboratory scale with comparatively low catalyst/substrate ratios, hydrogenation of the stabilising ligand is competitive with the desired process, particularly when COD is employed.[27] On a larger scale with commensurately higher ratios, this is less so.[28]

Given these precedents,[29] NBD has provided a benchmark for study of diene reductions; reactive intermediates in the addition of H_2 to NBDRh-$(PPh_3)_2BF_4$ in CH_2Cl_2 have been studied.[30] In our own monitoring of the uptake of hydrogen by NBD, it was observed that catalysis by complex **3** showed successive fast and slow phases for the two stages. By contrast, the first phase in catalysis by complex **4** was slower than the second phase. Hydrogenation of NBD with various $P_2Rh(NBD)$ complexes has been studied by Heller et al., and variability of the rates of hydrogenation of the first and second double bonds



was observed and interpreted in their work.[31] The postulated course of deuterium addition to NBD,[32] catalysed by complexes **3** or **4**, was re-examined and confirmed in the present work. The ^{2}H NMR of the fully reduced norbornane (NBA) shows equal amounts of *exo*- and *endo*-deuteration at the 2,3,5,6-positions. As also previously indicated,[20] the first step occurs to produce *endo*-d_2-norbornene. The initial *endo*-hydride addition product is related to an intermediate that has been characterised.[33] Hence the first deuteration occurs from the *endo*-direction and the second is *exo*-specific, now specifically confirmed by ^{1}H, ^{13}C and ^{2}H NMR spectroscopy. After the first addition step, dissociation/recoordination occurs selectively to the *exo*-face of the monoene, to which H_2/D_2 is preferentially delivered.

A different result was obtained when Crabtree's iridium catalyst **5** was used to catalyse deuterium addition, albeit in the non-coordinating solvent CH_2Cl_2. In this case the 2,3-*exo*-dideuterated isomer of **2** predominated by 5:1. This implies a requirement for dissociation of NBD prior to addition. Since accumulated evidence demonstrates a stronger tendency for dihydrogen coordination to iridium compared to rhodium,[34] the reacting diene must dissociate and reassociate subsequent to priming of the metal centre with hydrogen. Mononuclear Ir polyhydrides are known, and can function as reactive intermediates.[35] This points to a radically different mechanism for hydrogenation with Crabtree-type catalysts, compared to their cationic rhodium diphosphine counterparts. Polyhydridic intermediates have been indicated in Ir complex-catalysed directed hydrogenation,[36] and postulated as intermediates in Ir complex-catalysed asymmetric hydrogenation.[37]

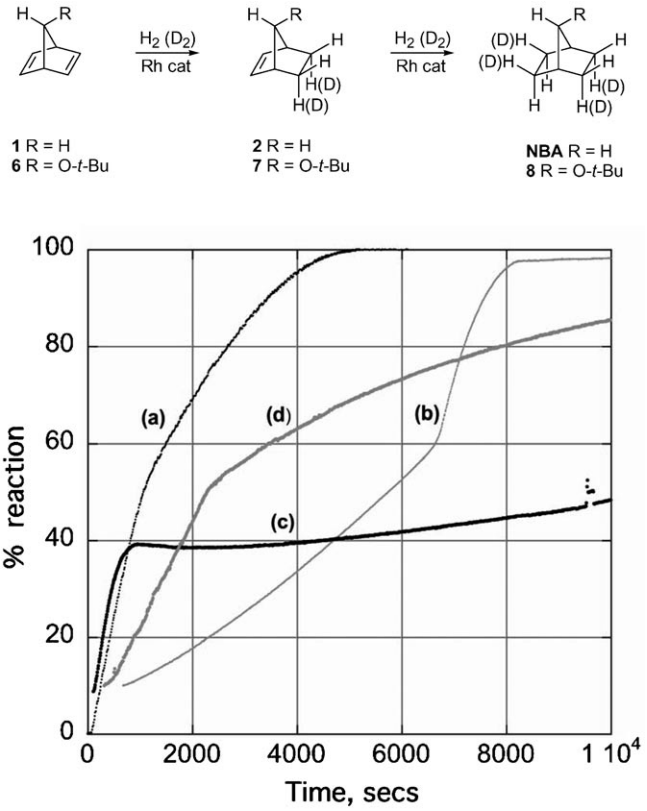


Figure 2. Hydrogen uptake in MeOH, 21 °C, 1.4 atm initial H_2; (a) 0.34 M **1**, 0.0016 M **3**; (b) as (a) with 0.0016 M **4**; (c) 0.48 M **6**, 0.0053 M **3**, complete reduction in 6×10^4 secs; (d) as (c) with 0.0053 M **4**, complete reduction in 2.5×10^4 secs. The data are not corrected for pre-hydrogenation in the warm-up period, patricularly affecting trace (c).

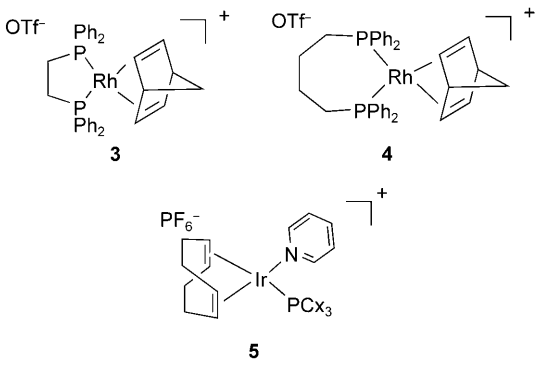
Hydrogenation of 7-*tert*-Butoxynorbornadiene

Homogeneous hydrogenation of 7-*tert*-butoxynorbornadiene **6** had not been carried out previously; in heterogeneous catalysis, both Pd-C catalysed and Pt-catalysed hydrogenation are specific for the *anti*-double bond.[38] In structurally characterised complexes, the *tert*-butoxy group is not innocent, and frequently provides an additional coordination site in an *exo*-alkene chelate.[39] In the present work, the reactivity of the two double bonds in diene **6** is dramatically different with both catalysts **3** and **4**, and the *syn*-alkene is rapidly reduced. Reduction of the remaining double bond is much slower, as indicated by the comparison with NBD shown in Figure 2. Using complex **3** as catalyst and stopping the reaction at *ca.* 60% completion provides exclusive formation of that the *anti*-product **7** in the first step. Carrying out the reduction with D_2 gave product **8** anticipated from NBD addition; the rapid first addition occurs to the *endo*-face of the diene and the second slower addition occurs to the *exo*-face. In the deuterated product the signals for *endo*-H2,H3, and *exo*-H5,H6,[40] were absent save for a trace of the latter (for full details of NMR spectra see the Supporting Information).

Hydroboration

The asymmetric hydroboration of NBD had been previously reported as part of H. C. Brown's classic work.[9] Later refinement of the original work provided a 62% yield of *exo*-norborn-2-en-5-ol **6** in 80% *ee* In their original demonstration of catalytic asymmetric hydroboration, Burgess and Ohlmeyer reported that the double hydroboration/oxidation of NBD using DIOP as ligand and an exess of catecholborane gave *exo*-2,6-diol as the major product in 76% *ee*[11] These results indicate that catalytic hydroboration of NBD is *exo*-selective in both steps, unlike hydrogenation. The present set of experiments, where catecholborane is not in large excess, show that the *exo-endo*

Table 1. Stereochemical course of hydroboration of NBD **1**.[a]



Entry	Catalyst (mol%)	Borane	Yield (%)	*endo*:*exo*
1	**A** (0.6)	**I**	85	1.0:21.7
2	**A** (8.3)	**I**	82	1.0:19.4
3	**A** (11.8)	**I**	78	1.0:14.0
4	**A** (26.3)	**I**	85	1.0:3.9
5	**A** (0.6)	**I**	75	1.0:16.3[b]
6	**A** (1)	**II**	80	1.0:9.0
7	**B** (1)	**I**	73	1.0:18.5
8	**C** (1)	**I**	77	1.0:30.2
9	**B** (1)	**II**	72	1.0:49.5
10	**C** (1)	**II**	75	1.0:43.0

[a] *Conditions:* NBD 0.3 mmol, borane 1 equiv., THF 1.5 mL (all 0.2 M in reactants), room temperature; catalyst **A** = [(*S,S*)-MeDuPhos]Rh(NBD)OTf, **B** = $[(NBD)RhCl]_2$, **C** = $(NBD)_2RhOTf$; **I** = catecholborane, 2 h; **II** = pinacolborane, 12 h; *endo*:*exo* ratios were determined by integrating the respective ^{1}H NMR signals at 6.44 and 6.16 ppm, see Supporting Information.

[b] 4 equiv. NBD relative to catecholborane were used.

product ratio for the first hydroboration step is strongly turnover dependent (see Table 1, entries 1–5). More *endo*-isomer is formed in the initial step than later, consistent with differentiation between the initial stoichiometric (*endo*-rich) and subsequent catalytic (*exo*-rich) stages. Pinacolborane also reacts with predominant, but less pronounced *exo*-selectivity (entry 6). Although (*S,S*)-MeDuPhos was employed as the ligand, the reactions were not significantly enantioselective (< 10% *ee*).

In an effort to divert hydroboration to the *endo*-face of NBD, ligand-free catalysts were employed (entries 7–10). Under these conditions a labile rhodium boride intermediate is involved, and for styrene *syn*-Rh–B addition followed by *syn*-Rh–H elimination leads to the corresponding β-vinylborane.[41] Since that outcome is not possible in a rigid cyclic system, a normal hydroboration route is anticipated and indeed observed. The results are similar to those with ligated catalysts (entries 7 and 8). When pinacolborane is used, the stereoselectivity is lower with catalyst **A** (entry 6), but higher with catalysts **B** or **C** (entries 9 and 10).

Hydrogenation of Cyclic Non-Conjugated Dienes

Cyclopentadiene Dimer

endo-Dicyclopentadiene **10** provides an interesting case. Hydrogenation proceeds smoothly in a two-phase process with either catalyst **3** or **4**, but the first step giving monoene **12** is much faster than the second in both cases. On deuterium addition the familiar pattern of *endo*-addition to the first double bond was observed. The second double bond is also hydrogenated cleanly and stereoselectively to the cycloalkane **11**, but interpretation of the results proved to be challenging, since the NMR spectra, both for ^{1}H and ^{2}H addition experiments, were more complex than expected. Chemical shift separation in the proton spectrum is small, and it required analysis at 700 MHz assisted by ^{13}C *J*-correlation in order to assign all the signals with confidence.[42] The addition of deuterium to diene **10** catalysed by complex **3** gave deuterated **11**. The near complete lack of an H8-*endo* signal at 1.23 ppm proved the key in assigning the course of the first addition. It proved impossible to analyse the deuterium distribution in the cyclopentane moiety completely by ^{1}H NMR. Clarification arose from analysis of the ^{2}H-coupled ^{13}C NMR spectrum, which revealed all four separate product carbon nuclei derived from the alkene double bonds because of their characteristic α- and β-isotope shifts.[43] *endo*-Dideuteration at the norbornene moiety is accompanied by *ca.* 5% of monodeuteration, unlike the clean addition seen in the bicyclo[2.2.1] series. (Figure 3).

For reduction of the cyclopentene double bond, at least six isotopomers can be identified by analysis of C4 of the ^{13}C NMR spectrum. The presence of 3,5-dideuterated species (6%) as well as small quantities of both 2- and 3-monodeuterated species requires H-isomerisation in an intermediate, as well as H/D exchange with the reagent. In addition, the formation of a substantial amount of the 3,4,5-trideuterated species indicates that this reaction intermediate must be able to exchange hydrogen isotope with external D_2. This exchange process also accounts for the incursion of some monodeuterated species at C7. Concurrent analysis of C3,C5 on the same sample reveals a small amount of dideuteration at C4, the signals of the relevant isotopomers being starred in Figure 2 (**B**). This observation requires that the initial addition to $\Delta_{3,4}$ in compound **10** is *exo*-stereoselective rather than stereospecific.

Further proof of *exo*-selectivity in hydrogenation of the cyclopentene double bond is afforded by the slow and incomplete hydrogenation of allylic ether **12**. The reaction effectively stops after reduction of the norbornene double bond, consistent with steric inhibition of coordination at the *exo*-face of the cyclopentene afforded by the OMe group.

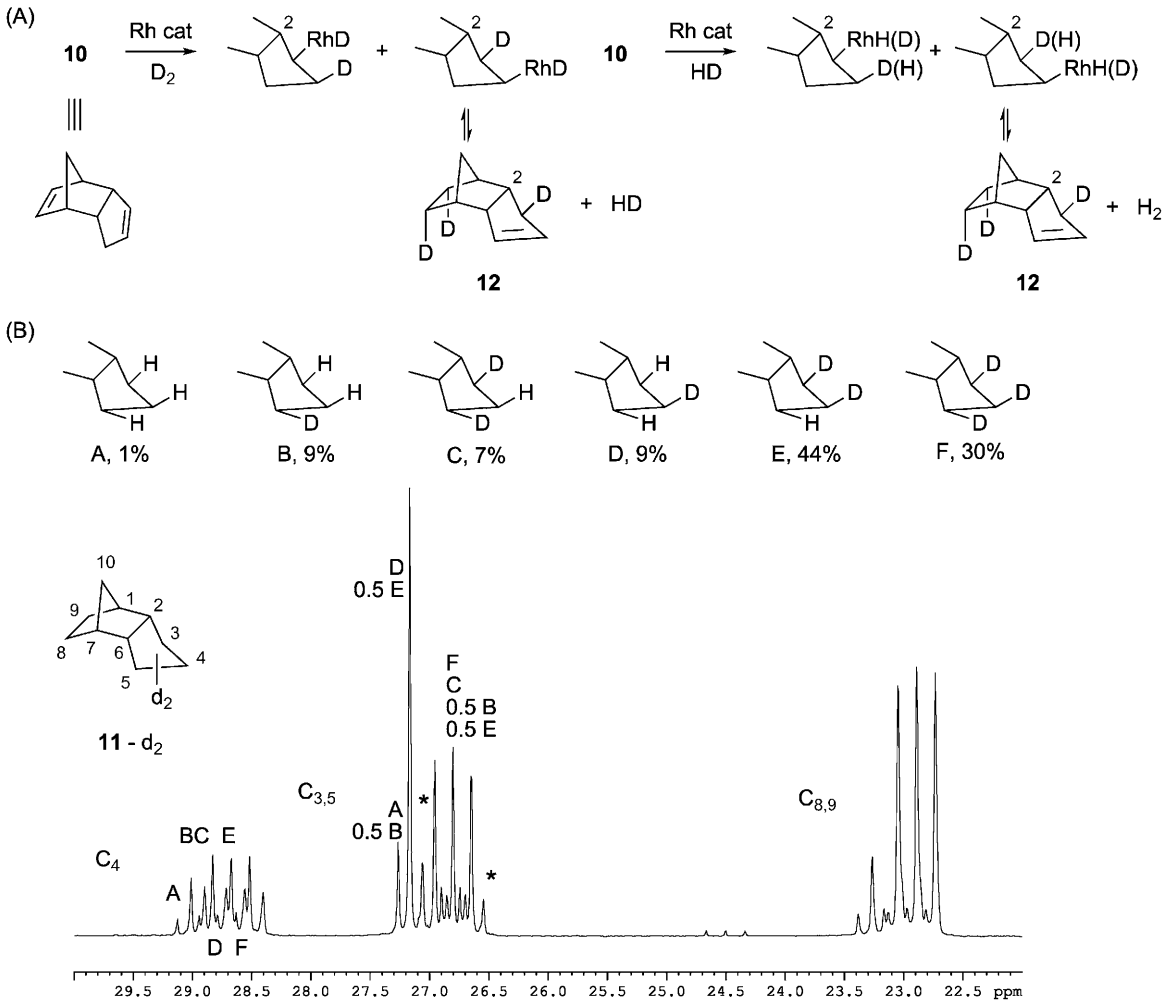


Figure 3. (**A**) Exchange pathways in D_2 reduction of the cyclopentene double bond of compound **10**; (**B**) isotopomer distribution in the ^{13}C NMR spectrum of the deuterated product **11**, C4, C3,C5, C8,C9 shown. The starred peaks indicate dideuterated C4 isotopomers.

endo-Dicyclopenta-4,8-dien-3-one

When the corresponding dienone **13** was hydrogenated, both steps, and particularly the second to form the saturated ketone **14**, were quite slow (Figure 4). A potential reason is made clear by analysis of the ^{31}P NMR spectrum of the Rh-DPPE solvate complex in CD_3OD with added **13**. This shows that the predominant species formed exhibits a characterisic eight-line multiplet associated with two distinct coordinated alkenes ($\delta_P = 59.6$ ppm, $J_{P,Rh} = 146$ Hz, $J_{P,P} = 20$ Hz; $\delta_P = 57.3$ ppm, $J_{P,Rh} = 138$ Hz). If the observed species is not the true catalytic intermediate and dissociation of the alkene from this species is required before hydrogenation, slow turnover can be explained.

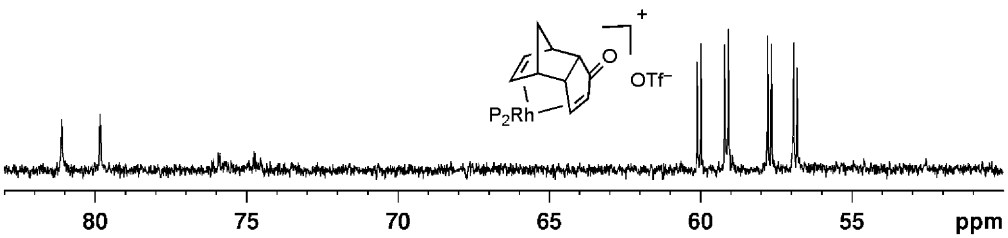
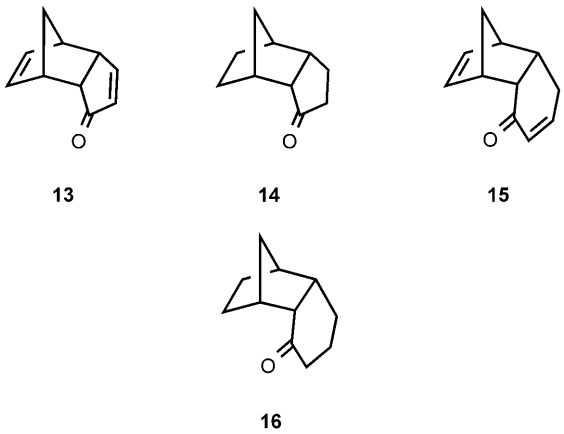


Figure 4. ^{31}P NMR spectrum of Rh-coordinated dienone **13** in the presence of hydrogenated catalyst **3**, CD_3OD, 298 K; $\delta =$ 59.6 ppm, $J_{P,Rh}$ 146 Hz; 57.3 ppm, $J_{P,Rh}$ 138 Hz, $J_{P,P}$ 19.5 Hz; P_2Rh solvate is present at $\delta = 80.5$ ppm.

Full analysis of the ^{1}H NMR spectrum of the first named product **14** was carried out, in order to make secure assignments in the corresponding D_2 addition experiment. On the basis of COSY, HMBC and HSQC spectra both the position and configuration of all hydrogens were established. There is considerable signal overlap, even at 500 MHz, but the *exo*- and *endo*-hydrogens of **14** related to the alkene of **13** may be identified. One anomaly is presented in comparison with hydrocarbon **11**. The two *endo*-hydrogens at C8 and C9 are quite dispersed, being at 1.30 and 1.63 ppm respectively (*vs.* 1.20 ppm in compound **11**). The deshielded member of the pair belongs to C9, and the effect arises from the anisotropic field of the C1 carbonyl group.[44] On addition of D_2 to the dienone **13** the ensuing ^{1}H NMR spectrum is much simpler, but shows nine rather than the expected ten protons. The reason for this is seen to be a second keto-enol promoted deuteration α- to the carbonyl group at C4, and this is clear from the ^{2}H NMR spectrum of the product, where the signal at 41.6 ppm corresponding to C2 is a pentuplet. Surprisingly, analysis of the ensuing ^{1}H NMR demonstrates that D_2 addition to both alkenes occurs from the *exo*-direction, characteristic of a norbornene pathway for reduction of the first double bond. The *endo*-protons at C5 and C9 remain intact, and are clearly visible in the ^{1}H NMR of deuterated product.



endo-Tricyclo[6.2.1.0^{2,7}]undeca-4,9-dien-3-one

Hydrogenation of the homologous dienone **15** is even slower than that of dienone **13**, ultimately giving the saturated ketone **16**.[45] Again, full assignment of the ^{1}H and ^{13}C NMR spectra of the final product was carried out, with the necessary aid of COSY, NOESY, HMBC and HSQC spectra. This sequence located and identified the six methylene carbons and associated proton pairs, including the anomalous carbonyl-induced deshielding of *endo*-H10, observed at 1.58 ppm in CD_3OD. The three remaining protons of the CH_2CH_2 bridge resonate between 1.37 and 1.22 ppm. It proved important to distinguish between protons at C6 (1.81 and 1.35 ppm) and C5 (1.90 and 1.75 ppm), and this was achieved through COSY and HMBC correlation spectra. Reaction of dienone **15** with D_2 catalysed by complex **3** resulted first in *exo*-addition to the norbornene double bond, as had been observed for the enone **14** described above. The second addition step also took place from the *exo*-direction revealed by the loss of *exo*-H5, but with some (subsequent) scrambling of the deuterium at C4 adjacent to the carbonyl group.

The stereochemical course of the first hydrogenation for the α,β-unsaturated ketones **13** and **15** differs from the three examples **1**, **6** and **10** described earlier, where reaction occurs overwhelmingly from the *endo*-direction. This indicates that η^2,η^2-coordination is not invariably advantageous during hydrogen addition to dienes, since the electron-poor enones dissociate from rhodium prior to transfer of H_2 (or D_2) to the norbornene double bond.

Asymmetric Hydrogenation of a Skipped Diene

The results obtained in the section "Hydrogenation of Cyclic Non-Conjugated Dienes" provide a guide for reduction of acyclic dienes, and demonstrate the independence of the two reaction steps. Hydrogenation of skipped dienes was the objective. To be useful in synthesis, the reaction needs to be chemoselective, with the first double bond reacting faster than the second. Dialkene chelation of the diene fragment during the first hydrogenation step is presumably responsible. When the central carbon is monosubstituted or unsymmetrically disubstituted, the first reaction step involves desymmetrisation; the product is chiral. Successful "*meso*-trick" experiments are quite rare in enantioselective hydrogenation,[46] although common elsewhere.[47] There are only a few structurally characterised 1,4-diene complexes, and the dialkene may coordinate with C_s symmetry or with C_2 symmetry.[48] With a C_2 symmetric ligand this gives rise to four different coordination modes as shown in Figure 5; the locally chiral forms iii) and iv) are of particular interest.

Penta-1,4-dien-3-ol **17a** is readily available and suitable for this purpose. In order to avoid the possible involvement of competing hydroxy-directed hydrogenation,[49] the related TBDMS ether **17b** was first employed as reactant (Figure 6). Hydrogenation occurred very rapidly in MeOH solution with a variety of catalysts, as shown in Table 2. It is clear that the first double bond was hydrogenated more rapidly

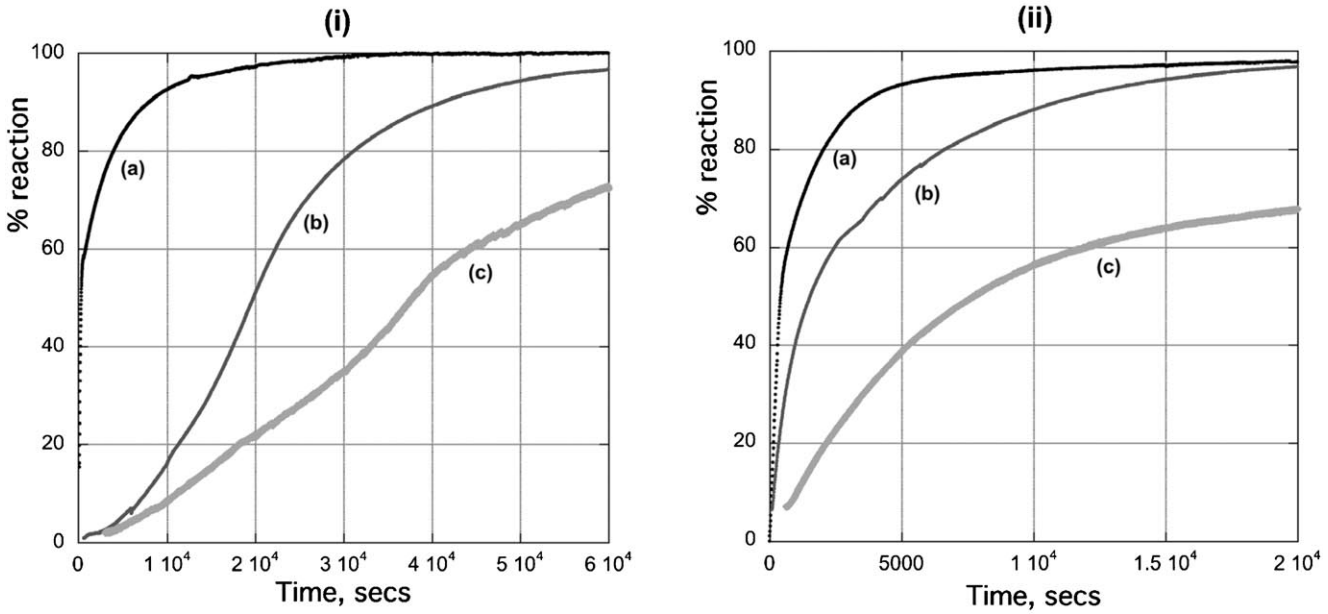


Figure 5. Hydrogen uptake in MeOH by **10**, **13** and **15**. 21°; (i) catalyst **3**; (**a**) cat 5.39 mM, **10** 0.57 M, H_2(init) 1.4 atm., **(b)** cat 2.64 mM, **13** 0.26 M, H_2(init) 2.0 atm, (**c**) cat 3.69 mM, **15** 0.33 M, H_2(init) 2.0 atm, complete reduction in 1.5×10^5 secs; (ii) catalyst **4** (**a**) cat 5.22 mM, **10** 0.59 M, H_2(init) 1.4 atm, (**b**) cat 5.17 mM, **13** 0.26 M, H_2(init) 2.2 atm, (**c**) cat 3.69 mM, **15** 0.36 M, H_2(init) 1.8 atm, $>90\%$ reduction in 8×10^4 secs.

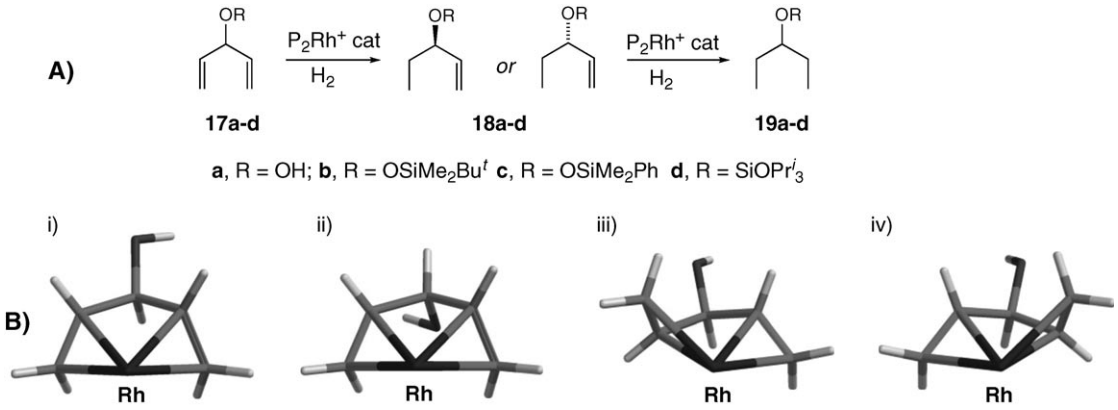
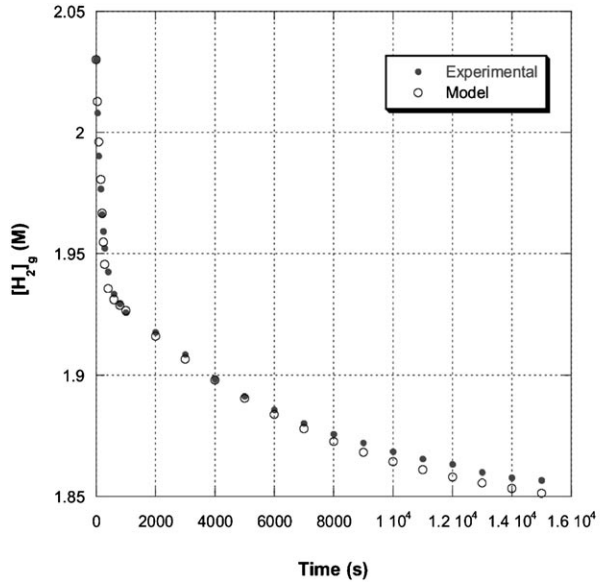


Figure 6. A) The reaction pathway in hydrogenation of 1,4-dienes **17** by rhodium diphosphine complexes, **B**) possible η^2,η^2 modes of diene coordination in **17a**; i), ii) C_s mode, iii) C_2 *Si*, *Si*, iv) C_2 *Re*, *Re*.

Table 2. Hydrogenation of dienol **17a** and its silyl ethers. < W = 3

Entry[a]	Ligand L_2	Reactant	Time [min]	**17**:**18**:**19**	*ee* [%] of **18**
1	Dppb	**17b**	10	0:100:0	–
2	(*S*,*S*)-Chiraphos	**17b**	5	0:100:0	20
3	(*S*,*S*)-Dipamp	**17b**	10	0:52:48	15
4	(*R*)-Binap	**17b**	10	12:68:20	ND
5	(*S*,*S*)-MeDuphos	**17b**	8	12:87.5:0.5	50 (*R*)
6	(*S*,*S*)-*i*-PrBPE	**17b**	20	0:50:50	ND
7[b]	(*S*,*S*)-MeDuphos	**17c**	15	13:62:25	47 (*R*)
8	Various as above	**17d**	–	No reaction	–
9	(*S*,*S*)-MeDuphos	**17a**	45	0:100:0	53 (*R*)

[a] *Conditions:* 0.136 mmol **17**, 1 mol% catalyst [RhL_2NBD]OTf, 1 mL MeOH, initial H_2 pressure 1.6 atm, 21 °C.
[b] In dichloroethane.



$H_2(g) \rightleftharpoons H_2(l)$ $k_{1f} = 2.99 \times 10^{-3}$; $k_{1r} = 1.013$

$Rh + S \rightleftharpoons RhS$ $k_{2f} = 5.405$; $k_{2r} = 1.06 \times 10^{-2}$

$RhS + H_2(l) \rightarrow Rh + I$ $k_3 = 10.634$

$Rh + I \rightleftharpoons RhI$ $k_{4f} = 1.577$; $k_{2r} = 4.03 \times 10^{-1}$

$RhI + H_2(l) \rightarrow Rh + P$ $k_5 = 1.203$

Rh = Catalyst
$H_2(g)$ = Hydrogen in gas phase
$H_2(l)$ = Hydrogen in solution

S = Diene
I = Monoene
P = Final product

Figure 7. Hydrogenation of 3-*tert*-butyldimethylsilyloxypenta-1,4-diene with the DipampRh$^+$ complex, Table 2, entry 3. Results of curve fitting for reaction in a constant volume hydrogenator according to the data shown, simulated by Berkeley Madonna (Kagi Software).

than the second in all cases, although the relative and absolute reactivities varied with the catalyst. The achiral DPPB complex gives complete reduction to the monoene **18b** without significant further reaction, as does Chiraphos, (entries 1 and 2). Standard methods for the determination of enantiomer excess did not work in this case. After TBAF-promoted desilylation, the ^{31}P NMR method introduced by Feringa et al. proved effective and was utilised in subsequent cases.[50] An *ee* of 20% was demonstrated this way for the reaction of entry 2. For entry 3, the reaction remains fast but less separation between the first and second steps was evident. This is also apparent in the BINAP case (entry 4) since starting material is present at the same time as both part-reduced **18b** and fully reduced product **19b**. Overall, the most promising results were obtained in entry 5 with (*S,S*)-MeDuphos as catalyst, where an *ee* of 50% (*R*) was observed accompanied by good chemoselectivity between the first and second steps.[51] This was followed up with a more detailed analysis of the course of reaction (Figure 7). The experimental data were fitted according to a kinetic model, taking into account substrate binding in both the first and second stages. The initial slope of the fast sector was *ca.* 10 times greater than the initial slope of the subsequent slow sector. With the more bulky (*S,S*)-*i*-PrBPE as ligand (entry 6), less distinction between the first and second steps was observed.

Changing the silyl group was less fruitful. With the corresponding dimethylphenylsilyl ether **17c**, rapid Rh-catalysed reduction was observed in MeOH, effectively stopping after the first step. The product isolated was the alcohol **18a**, however. It was demonstrated in a control experiment that addition of the (*S,S*)-Chiraphos catalyst (5 mol%) to a solution of **17c** in CD_3OD and monitoring by ^{1}H NMR led to desilylation within 5 min. In $ClCH_2CH_2Cl$, this side reaction did not occur and enantioselective hydrogenation of **17c** was observed albeit with lower chemoselectivity (entry 7). The corresponding TIPS ether **17d** proved unreactive towards H_2 (entry 8), presumably demonstrating the severe steric bulk of the silane. Finally, hydrogenation of the parent alcohol **17a** was studied, since the observed reduction of **17c**, appeared to involve prior desilylation. This occurred smoothly, and effectively stopped after the first step, giving **18a** in 53% *ee* (entry 9)!

Since the nature of the substituent has little effect on the *ee*, a directing effect is unlikely. The distinct chemoselectivity favouring the first step militates in favour of a reactive intermediate in which both double bonds remain coordinated. Four alternative conformations of the coordinated diene are accessible (Figure 6), and there is no evidence to indicate whether the C_2 or C_s forms are preferred. The accessibility of C_2-symmetric forms **C** and **D** provides the opportunity for chiral discrimination on co-complexation with a C_2-symmetric diphosphine ligand, and this would play a part in the overall selectivity observed.

Conclusions

Even the simplest hydrogenations can exhibit complex pathways. The stereochemical course of reduc-

tion of the norbornene double bond in a series of dienes is dependent on the environment of the second double bond. For chelating dialkenes **1**, **6** and **10**, the first reduction step occurs from the *endo*-direction with rhodium (but not iridium) catalysts, in accord with the Chelate type reactions shown in Figure 1. Where the dialkene bears an electron-withdrawing carbonyl group, reaction is far slower and in accord with the Open type reactions of Figure 1. It was also observed that the bridge substituent in dialkene **6** strongly affected the regioselectivity of the first reduction step. Deuterium addition revealed rapid H-shifts that occurred during the second step of reduction of dicyclopentadiene **10**. In contrast, catalytic hydroboration of **1** occurs predominantly from the *exo*-direction, but extrapolation of results at low turnover indicates that the initial step is *endo*-selective. This indicates that the reagent competes successfully with the for the second coordination site of dialkene chelation.

The selectivity observed in reduction of chelating cyclic dienes may be applied to hydrogenation of *meso*-1,4-dienes. The results obtained demonstrate good control of chemoselectivity, with the first step occuring significantly faster. Modest *ee*s are obtained, indicating the benefit of further study.

Experimental Section

General Hydrogenation Procedure

Hydrogenations were performed in a modified Schlenk tube that had been fitted with an RS 286–670 differential pressure transducer from RS Components. The pressure transducer signal output was connected to an ACD+16 data-logger from Pico Technology Ltd, which in turn was connected to an IBM PC compatible computer running PicoLog software from the same company, *via* an RS232 connector (Figure 8). The pressure transducer measured the difference between the pressure inside and outside the vessel in the range of 0–30 psi, corresponding to output signal range of 0–100 mV. It was calibrated prior to use against atmospheric pressure and high vacuum. The ACD+16 data-logger delivers a ± 5 V power supply to the transducer and receives readings from the sensor, logging these data to the IBM PC computer every five seconds.

A modified Schlenk line was used with the hydrogenation vessels. The normal vacuum/argon outlets were connected to a three-way Swagelok® valve which allowed switching connection between vacuum/argon or hydrogen (steel line fitted with pressure control gauge) and the vessel.

The reaction vessel was assembled and charged with hydrogen at 2.0 atm pressure. Insignificant voltage decrease in reading from the pressure transducer after 24 h indicated that the vessel was sufficiently sealed for experiments.

The general procedure for pressure-monitoring hydrogenation follows the procedures described below.

Reactants, catalyst and degassed solvent were transferred to the vessel under argon and the vessel was fitted with the pressure transducer. The reaction mixture was cooled to

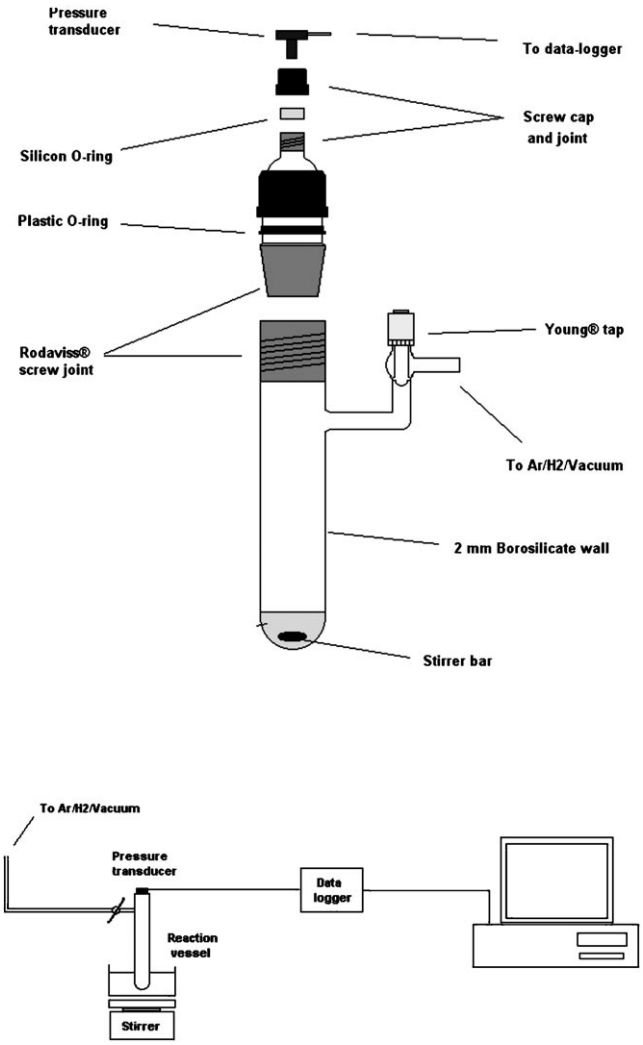


Figure 8. The experimental set-up for hydrogenation reactions, conducted in constant volume apparatus.

−78 °C and evacuated under high vacuum with vigorous stirring. Hydrogen was charged at a specified pressure, and then evacuated under high vacuum. This process was repeated twelve times to ensure saturation of hydrogen in the solution. Hydrogen was finally charged to the specified pressure and the Young's tap was sealed. The reaction mixture was allowed to warm up without stirring to room temperature using a water bath. Pressure within the vessel was allowed to equilibrate. The computer monitored and recorded the readings of the pressure, which were displayed in a voltage *vs.* time graph. The reaction mixture was stirred vigorously at ambient temperature (21 °C) in the water bath until completion, as indicated by on-screen monitoring. Reaction was stopped by venting excess hydrogen. In many cases, the reaction was performed in CD_3OD and NMR spectra of the crude mixtures were recorded directly without any work-up. When other solvents were used, the reaction mixture was filtered through a short pad of silica using dichloromethane as eluent before solvents were evaporated under vacuum to give the products.

Typical Procedure for Asymmetric Hydrogenation (17b, entry 5, Table 1)

The starting material was prepared as previously described.[52] The hydrogenation vessel (Figure 8) was charged with diene **17b** (0.027 g., 0.136 mmol) and complex {Rh-[(*S,S*)-MeDuphos]NBD}OTf (0.65 mg, 0.01 equiv., from stock solution in MeOH?) in MeOH (1.0 mL). After equilibration under H_2 as described above, the reaction mixture was stirred for 8 min. After standard work-up the product 3-*tert*-butyldimethylsiloxy-1-pentene,[53] containing 12% of unreduced starting material, was dissolved in THF (2 mL.) and added dropwise at 0 °C to a 1 M solution of tetrabutylammonium fluoride in THF (1.36 mL). The solution was stirred at 0 °C for 1 hour and allowed to warm up to room temperature. It was then taken up in diethyl ether (20 mL) and washed with brine solution (3 × 10 mL). The organic solution was dried over magnesium sulfate and solvent evaporated to give 1-penten-3-ol as the main product, which was dissolved in $CDCl_3$ and used directly in the next step. To this solution was added pyridine (11 μL, 0.134 mmol) and PCl_3 (4 μL, 0.045 mmol) at room temperature. The reaction mixture was stirred for 30 min. and the ^{31}P NMR was taken directly (see Supporting Information for full details of *ee* determination).

Acknowledgements

We thank the Clarendon Fund (Oxford) and Balliol College for Scholarships (to BN) as well as the Leverhulme Foundation for a fellowship (to JMB). Johnson-Matthey kindly provided a loan of precious metal salts. We thank the CRL NMR Facility and Dr. T. D. W. Claridge and Dr. B. Odell for their help.

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